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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,767	01/16/2004	Hector F. DeLuca	1256-00935	6302

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EXAMINER	
QAZI, SABIHA NAIM	
ART UNIT	**PAPER NUMBER**
1612	

MAIL DATE	DELIVERY MODE
12/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/758,767	DELUCA ET AL.	
	Examiner	Art Unit	
	Sabiha Qazi	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/29/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7,9,12-15,22-26,29-32,35-38 and 41-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4, 7, 9, 12-15, 22-26, 29-32, 35-38, 41-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Final Office Action

Claims 1, 3, 4, 7, 9, 12-15, 22-26, 29-32, 35-38, 41-51 are pending.

Amendments are entered. No claim is allowed.

Summary of this Office Action dated December 03, 2008

1. Continued Examination Under 37 CFR 1.114
2. Double Patenting Rejection
3. Response to Remarks
4. Communication

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/29/08 is entered.

Double Patenting Rejection

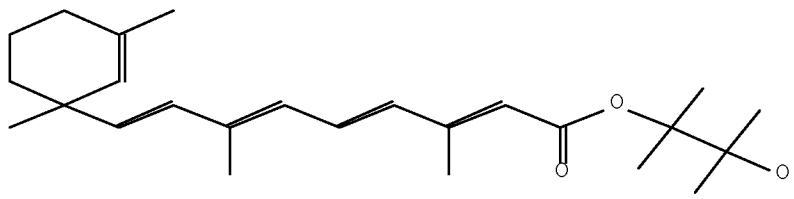
1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. 1, 3, 4, 7, 9, 12-15, rejected on the ground of nonstatutory double patenting over claim 18 of U. S. Patent No. 7,126,017 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: The compound t-butyrate ester retinoyl t-butyrate is an elected species and has been disclosed in lines 45-50 in column 18 of US '017. This is a double patenting rejection. Specific compound has been disclosed in claim 9 and 14 of the present application. A method for reducing the toxicity has been claimed using the same compound disclosed in claim 18 of US '017.



DCR-942545
CN.S 9-(1,3-Dimethyl-cyclohex-2-enyl)-3,7-dimethyl-nona-2,4,6,8-tetraenoic acid 2-hydroxy-1,1,2-trimethyl-propyl ester

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 3, 4, 7, 12, 13, 20-22, 26, 29-32, 35-38 and 43-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for supporting the growth of vitamin-A-deficient rats by 1-t-butyl-RA (elected species), does not reasonably provide enablement for all the treatments of diseases as has been claimed in claims 20 and 43 and also the compounds as claimed in claim 1. The diseases include proliferative skin disorders characterized by abnormal cell proliferation or cell differentiation e.g. dermatitis, eczema, keratosis, acne and psoriasis and for the treatment of neoplastic diseases such as skin cancer, colon

cancer, breast cancer, prostate cancer, lung cancer, ovarian cancer, neuroblastoma, and leukemia as well as for the treatment of skin conditions such as wrinkles, lack of adequate skin firmness, lack of adequate dermal hydration, and insufficient sebum secretion. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re

Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1) Nature of the invention

The instant claims are directed to retinoid compounds and methods of treating various diseases including different types of cancers. Thus, the breadth of the claim is very large. The invention is also drawn to the

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[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

compounds and the method of minimizing or reducing the toxicity of a retinoid having a free carboxyl group and the resulting modified retinoid are described. The modified retinoid compounds are useful in the treatment and prophylaxis of all diseases and disorders where retinoid compounds have been shown effective.

2) **The breadth of the claims**

Claims 20 and 43 are broad because (1) it contains the treatment of abnormal cell proliferation or cell differentiation e.g. dermatitis, eczema, keratosis, acne and psoriasis and for the treatment of neoplastic diseases such as skin cancer, colon cancer, breast cancer, prostate cancer, lung cancer, ovarian cancer, neuroblastoma, and leukemia as well as for the treatment of skin conditions such as wrinkles, lack of adequate skin firmness, lack of adequate dermal hydration, and insufficient sebum secretion. (2) Claim 1 is broad because it contains large number of compounds which has different structures so are expected to possess different properties.

3) The state of the prior art: There is no reasonable predictability and no established correlation between in vitro activity and the treatment of

diseases as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any compound as a pharmaceutical composition on its face.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled. The reference Chandraratna et al., EP 0337,689 A1 (IDS reference) teaches that retinoid compounds are useful for the treatment of dermatoses. The reference does not teach the treatments of various cancers and other diseases as presently claimed. Furthermore, it is not possible to predict the treatment of any of the claimed diseases of large number of compounds as in claim 1 and their uses for the treatments of diseases as in claim 20 and 43.

5) The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for practicing the claimed invention in its “full scope”. No reasonably specific guidance is provided concerning useful therapeutic protocols.

The instant disclosure provides no evidence to suggest that this unique activity can be extrapolated to tumors having unrelated mechanisms of resistance, and thus does not meet the "how to use" prong of 35 USC 112, first paragraph with regard thereto. The inventor provides very little direction in the instant specification. The instant specification does not have any working examples with respect to the various substituents as given above. The state of the art indicates that even when the reactants are similar, and the reaction conditions are the same, it is not necessary that it would form the same products.

6) **The quantity of experimentation necessary**

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used for the treatment of various type of cancers as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the claimed invention in its "full scope" a person of ordinary skill in the art would

have to engage in undue experimentation, with no assurance of success.

The instant specification teaches that these compounds can be used for the treatments such as proliferative skin disorders characterized by abnormal cell proliferation or cell differentiation e.g. dermatitis, eczema, keratosis, acne and psoriasis. They should also be especially useful for the treatment of neoplastic diseases such as skin cancer, colon cancer, breast cancer, prostate cancer, lung cancer, ovarian cancer, neuroblastoma, and leukemia as well as for the treatment of skin conditions such as wrinkles, lack of adequate skin firmness, lack of adequate dermal hydration, and insufficient sebum secretion, see [0050] on page 8.

Response to Remarks

Terminal disclaimer has been filed on 3/31/08 has been not been approved. Examiner will withdraw the rejection when TD will be approved by the office. DP rejection is now maintained. The amount of direction or guidance provided and the presence or absence of working examples

Allowable subject matter

Claims 9, 14 and 15 are not taught by the prior art. These are not allowed because double patenting rejection is still maintained. However, closest prior art is TSUTSUMI, YOICHI reference (abstract of JP9185159, IDS reference). Instant claims differ from the reference in three ways. First the side chain is attached to a different position of retinoic acid ring; second double bond is at different positions of the ring; third, one extra methyl group at the retinoid ring. The reference and prior art of record does not teach nor suggest such retinoic acid derivative as has been presently claimed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is (571) 272-0622. The examiner can normally be reached on any business day except Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sabiha Qazi/
Primary Examiner, Art Unit 1612